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A N  
EXPERIMENTAL ESSAY,  
O N  
THE MANNER IN WHICH OPIUM ACTS ON  
THE LIVING ANIMAL BODY.

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B Y  
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## INTRODUCTION.

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**M**ANY of the first physiologists, both in Great Britain, and other countries, have endeavoured to ascertain the manner, in which opium acts on the living animal body ; and to their assiduity we are indebted for a vast number of experiments on this subject.

But the inferences, which one author makes from his observations, generally contradict those of another ; and the perplexity, arising from this source, is increased, by each having brought forward his

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own

own experiments and conclusions, without comparing them with those, which had been made by others.

That I may avoid this error, I shall introduce the following paper, with a concise view of the state of our knowledge, concerning the action of opium on living animals, at the time my own experiments were begun. And, not to swell this part of the paper, by relating the arguments which each writer has used, in support of his own hypothesis, or against those of others ; or by giving any account of experiments, since proved inaccurate, I shall merely collect together the few seeming facts which remain, after rejecting the useless and inconsistent observations, in which they have been involved by the ingenuity of authors, and their partiality for particular opinions.

In various writers, we find the effects of a moderate dose of opium, on living animals, accurately described ; most people have experienced them, indeed, in their own persons.

Soon after its exhibition, it renders the pulse quicker and fuller, it produces relief from pain, and, in most instances, tranquillity of mind, and refreshing sleep.

The effects of opium, like those of other drugs, become less considerable, the longer the body is accustomed to it. Every person knows, what quantities of opium are consumed by the inhabitants of many eastern countries. And even in our own, we are every day meeting with people, who have habituated themselves to a very free use of it. I have seen a man drink four ounces



of laudanum, without perceiving from it even a tendency to sleep.

Dr. Mead is among the earliest authors, who have given an accurate account of the effects of an over-dose of opium.

In his Treatise on Poisons, first published in 1702, he relates the following experiment made on a dog. “ When he had thus  
 “ taken (says he), as I could guess, near  
 “ two drams of the solution, I watched  
 “ him about an hour; then he began to  
 “ sleep, but presently started up with con-  
 “ vulsions, fell into universal tremblings,  
 “ his head constantly twitched and sha-  
 “ king; he breathed short and with la-  
 “ bour, lost entirely the use, first of his  
 “ hinder legs, then of his fore ones, which  
 “ were stiff and rigid like sticks. As he lay  
 “ snorting, to hasten his end, I was giving  
 “ him

“ him more of the solution, but, on a sudden his limbs grew limber and he died.”

Tralles, in his elaborate work, *De Usu Opii*, gives nearly the same account of the effects of an over-dose of opium. But, as he describes these effects, such as he accidentally met with them, in the human body, his account of them is more interesting than that of most other authors. “ Me-  
 “ mini (he observes) horrendis convulsio-  
 “ nibus affectum infantulum ; cui, per er-  
 “ rorem, datus fuerat pulvillus, matri def-  
 “ tinatus, granulum forte dimidium, ex-  
 “ tracti opii, habens.” He quotes several other similar cases from different authors.

The convulsions, produced by an over dose of opium (it has since been observed), are of a peculiar kind. In many respects,

they greatly resemble tetanus. They are of that species, which has been termed tonic ; have intermissions, and during these, are renewed by the slightest touch. I have repeatedly seen them excited by a person walking across the room, while the animal lay on the floor ; and have always observed the convulsions from an over-dose of opium, in frogs and rabbits (the only animals on whom I have made the experiment), assume the form of a true opisthotonos, without having ever perceived in them the least tendency to any other form of tetanus.

Dr. Alston, by means of the microscope, observed the velocity of the circulation suddenly diminished, on throwing a watery solution of opium into the stomach of a frog : But he has not stated



ted accurately, the time required for producing this effect.

He has also observed, that certain effects of opium, if it be given in large doses, very suddenly follow its exhibition. It has almost instantly produced sleep, relief from pain, from tenesmus, from vomiting, &c. From such observations, Dr. Alston draws a very fair conclusion, that opium is capable of acting on the system in general, through the medium of the nerves, to which it is directly applied,

He has likewise shown, that a solution of opium, injected into a vein, produces the same effects, as when received into the stomach. In small quantity, it occasions no remarkable symptom; injected more freely, convulsions and death. It has been farther observed by various authors,

that opium, applied to the brain, or injected into the heart and blood vessels, produces convulsions more speedily, than when exhibited in any other way.

Dr. Alston found that opium thickens the blood, when mixed with it out of the body. It was a similar observation, which gave rise to the hypothesis of its occasioning death, by congealing the blood in the heart and large vessels. His paper on opium is in the 5th volume of the Edinburgh Medical Essays and Observations.

Such was nearly the sum of our knowledge, concerning the action of opium on the living animal body, when Dr. Whytt published his treatise on this subject.

In

In stating the additional information which he gives us, I shall pass over, in silence, certain conclusions, which, it may seem at first sight, I ought to have mentioned. On comparing them with the observations of later writers, however, they will be found inaccurate. His conclusions, for instance, concerning the manner, in which opium, applied to a distant part of the body, affects the motion of the heart.

These are more generally known, and have been more frequently referred to, than perhaps any other part of his treatise, notwithstanding they were, in a great measure, invalidated by the observations of Dr. Monro, as early as 1761; and have since been completely refuted, by a very accurate experiment of Fontana's, made on a large scale. As this experiment is re-  
lated

lated in the Appendix to his work on Poisons, and consequently not referred to in the General Index, it has often been overlooked. In a treatise lately published, on the influence discovered by Galvani, the author, in one part of his work, builds much of his reasoning on the conclusions of Dr. Whytt, which are here alluded to.

Dr. Whytt, as well as Haller, found the motion of the heart little affected, by the application of a watery solution of opium to its external surface. But the former shewed, contrary to an opinion which once prevailed, that the heart is far from being wholly exempted from the action of opium: And, what may seem curious, he found, that a solution of this drug, thrown into the stomach and intestines of a frog, affects its motion  
more



more speedily than decollation, and the destruction of the spinal marrow; and, on the other hand, that a large dose of opium destroys the voluntary motions of this animal, in a shorter time than cutting out the heart.

Dr. Whytt farther observed, that opium, thrown into the stomach and intestines of a frog, or merely applied to its abdominal muscles, produces effects less powerful and sudden, than when injected into the cavity of the abdomen.

Upon the whole (he remarks), opium produces all its effects most speedily on those animals, which cannot live long without a fresh supply of food and air.

By many of the experiments just alluded to, as well as by others, he confirms

Dr.

Dr. Alston's opinion, that opium produces many of its effects, through the medium of the nerves, to which it is directly applied. To this action of opium probably is to be attributed the following fact, the last I shall mention, from Dr. Whytt's treatise, namely that opium, injected into the great guts of a dog, affects the hinder extremities, more speedily than the fore ones.

I cannot, however, conclude my observations, on what this subject derived from the labours of Dr. Whytt, without quoting from his paper the following passage, which, as far as I can judge, either from my own experiments, or from those of others, contains one of the justest, and, at the same time, one of the most important observations, concerning the ac-  
tion

tion of opium on living animals, I have any where met with.

“ It remains (says he), therefore, that  
 “ opium, by affecting the extremities of  
 “ the nerves of the part to which it is ap-  
 “ plied, does, by means of their connection  
 “ and sympathy with the brain and spinal  
 “ marrow, destroy or prevent, through the  
 “ whole nervous system, the operation of  
 “ that power, upon which depends sensa-  
 “ tion and motion in the bodies of ani-  
 “ mals.” It is to be remarked, that Dr. Whytt does not here speak of the sympathy of nerves, but of their connection with the brain and spinal marrow.

Not long after the publication of Dr. Whytt's treatise, Dr. Monro published his observations on the same subject, in the 3d volume of the *Essays and Observations*,  
 Physical

Physical and Literary, of the Philosophical Society of Edinburgh.

Dr. Monro shews, that opium, applied externally, produces the same effects, as when thrown into the stomach and intestines, cavity of the abdomen, or blood vessels. He observes, page 306, “ The effects are, however, more speedy, where  
“ the dose is equal, when the opium is  
“ applied inwardly, than when applied  
“ outwardly ; as might have been presumed, from the greater sensibility and  
“ delicacy of the inward organs.”

He has also shewn, that, although opium, applied to a naked muscle, very suddenly destroys its power of contraction, yet, applied externally to a limb, while the skin is entire, it does not affect its muscles  
more



more speedily, or in a greater degree, than the muscles of any other part of the body.

Having observed the effects of opium on the entire animal, he wished to ascertain its effects, when it acts merely on the part to which it is directly applied.

“ But here (he observes), we perceive an obvious difficulty; for, if we stop the circulation in every part of the body, by cutting out the heart, or stop it in one particular part; it is evident, that the animal will be dead, or the nerves will have lost their energy, in a great measure, if not entirely, before the solution of opium can produce its effects in a very observable manner.”

This difficulty, however, was obviated in  
the

the following manner : Dr. Monro found, analogous to an observation of Dr. Alston, that, on pouring 30 drops of a strong solution of opium, through a hole made in the abdomen of a frog, the motion of the heart is so suddenly affected, that, in the space of two minutes, it beats with only half its usual frequency, and that, soon afterwards, all the muscles of voluntary motion are convulsed.

“ Having, by this last experiment (he  
 “ observes), discovered a method by which  
 “ this animal (the frog) is affected to a  
 “ violent degree with opium, in a shorter  
 “ time, than that in which the energy of  
 “ its nerves is considerably impaired, by  
 “ putting a stop to the circulation; I could  
 “ now determine, with certainty, whether  
 “ this animal could be affected in that vio-  
 “ lent degree, through the nerves to which  
 “ the

“ the opium was primarily applied, inde-  
 “ pendent of absorption, and the circu-  
 “ lation of the blood, by cutting out the  
 “ ventricle of the heart, and so stopping  
 “ the circulation, before I poured the  
 “ solution into the cavity of the abdo-  
 “ men; and on several trials, I found,  
 “ that the animal was in this way affect-  
 “ ed as in the last experiment,” (*i. e.* the  
 animal was convulsed); “ with this only  
 “ difference, that it required a somewhat  
 “ longer time to produce these effects in  
 “ the same degree.

The author, in his comment on this  
 experiment, observes, “ As the animal  
 “ was convulsed, and in a short time kill-  
 “ ed, by pouring the solution into the  
 “ cavity of the abdomen, after cutting  
 “ out the heart, we have undeniable evi-  
 “ dence, that there is a possible way of

B

“ applying

“ applying opium, so that it may produce  
“ those effects, through the nerves, to  
“ which it is primarily applied, indepen-  
“ dent of its absorption and circulation  
“ with the blood, as Dr. Whytt, from a  
“ similar experiment, first endeavoured to  
“ prove.”

Dr. Monro has also shewn, that the same effects are produced by throwing the solution of opium into the heart, while the heart itself is instantly rendered paralytic.

“ When we compare that part of the  
“ foregoing experiment which relates to  
“ the heart, (says the author), with some  
“ experiments made by Dr. Whytt,  
“ where the opium was applied to its  
“ outer part, we see how greatly the de-  
“ licacy of feeling of the inner side of  
“ the



“ the heart exceeds that of the outer  
 “ side.” And in another place he ob-  
 serves, “ We see how suddenly the whole  
 “ body sympathises with the heart.”

On looking over notes which I took  
 from his lectures in 1789, I find it men-  
 tioned, that although the aorta be pre-  
 viously cut, a solution of opium thrown  
 into the heart affects every part of the  
 body. And in a late paper, entitled,  
*Experiments on the Nervous System with*  
*Opium and Metalline Substances, made chiefly*  
*with the view of determining the Nature and*  
*Effects of Animal Electricity*, he observes,  
 “ Many years ago, I found, after cutting  
 “ the venæ cavæ and aorta of a frog, that  
 “ a watery solution of opium, poured into  
 “ the heart, occasioned in a few minutes  
 “ convulsions in its legs ; and after cutting

“ out the heart, that the opium poured  
 “ into the cavity of the abdomen affected  
 “ the legs in like manner; although, in  
 “ these experiments, the circulation was  
 “ not only interrupted, but the greater  
 “ part of the blood evacuated. I there-  
 “ fore then concluded, and now conclude,  
 “ that opium and other poisons, even af-  
 “ ter they are mixed with the mass of  
 “ blood, produce their fatal effects chiefly,  
 “ and almost solely, by acting on the  
 “ nerves of the heart and vascular system.”

Yet Dr. Monro found, that opium, ap-  
 plied to the extremities, is not capable of  
 affecting the whole system through the  
 medium of the nerves.

But the most important point concern-  
 ing the action of opium on living ani-  
 mals, established by this author, is its  
 being

being received into the system by means of the absorbents: which, as far as I can judge, he proves incontestibly, by shewing that the effects of opium, applied to a limb, after all communication between it and the rest of the body, by means of the nerves, is cut off, are soon felt in every part of the system.

Such are the circumstances relating to the action of opium on the living animal body, ascertained by Dr. Monro. The following conclusions, which I shall give in his own words, contain the leading opinions he formed on this subject.

“ We may indeed perceive, (says he),  
 “ that the effects of all the foregoing me-  
 “ dicines, (among which opium is inclu-  
 “ ded), when they are applied to the  
 “ found outer surface of the body, are  
 B 3 “ chiefly

“ chiefly owing to their absorption, mix-  
 “ ture, and conveyance with the blood ;  
 “ since they operate as violently, and  
 “ nearly as soon, when the nerves of the  
 “ part to which they are applied are cut,  
 “ as when they are entire.

“ If, again, they are applied to the  
 “ more sensible inward surface of the  
 “ primæ viæ, they may probably operate  
 “ more speedily, and in some cases more  
 “ violently, through the nerves alone,  
 “ than by their being absorbed, and con-  
 “ veyed by the blood.”

In another place he observes, “ As the  
 “ opium has a surprising influence over  
 “ the heart and arterious system, when  
 “ directly applied to them, and these ef-  
 “ fects, though greater, are similar to the  
 “ effects of this medicine when absorbed,  
 “ we



“ we may infer, that when it is abforb-  
 “ ed, mixed, and conveyed with the  
 “ blood, its effects are almoſt ſolely to be  
 “ aſcribed to its operation on the nerves  
 “ of the heart, and veſſels through which  
 “ it is carried; and, by analogy, the  
 “ like is probable of many other medi-  
 “ cines.”

In his 12th corollary, he remarks,  
 “ We are to conſider, that the nerves of  
 “ the heart, and large branches of the  
 “ vaſcular ſyſtem, affected by medicines  
 “ abſorbed and conveyed by the blood,  
 “ will influence by ſympathy other nerves  
 “ of the body, to which theſe medicines  
 “ may not be able to penetrate through  
 “ the very ſmall veſſels.”

“ But (he obſerves in another of his  
 “ corollaries) it is difficult to determine

“ whether we are to ascribe the chief effects of opium on the sound animal to its action on the nerves, to which it is immediately applied, or to its absorption.”

I shall quote but one more observation from Dr. Monro's paper. It deserves particular attention. That part of it which relates to opium, indeed, is suggested by what has already been said, namely, “ That the effects of an over-dose of opium, as well as of some other medicines, on frogs, are analogous to their effects on men and quadrupedes.”

Fontana, the well-known Italian physiologist, makes a similar remark. This author, among numerous experiments relating to other subjects, has made many with opium on living animals.

Only

Only a small part of what he has done on this subject, however, falls to be taken notice of here. He does not seem well acquainted with what had been ascertained by the physiologists of this country; before he published his experiments; and frequently bestows much pains endeavouring to prove, what has already been stated, as proved by others,

His experiments, indeed, seem accurate, and many of them are made on a scale even more extensive than was necessary for ascertaining what he had in view; but he draws few conclusions; and the imperfect manner in which most of the experiments are related seldom admits of any, but those which the author makes from them.

This doubtless proceeded from his having

ving in view to prove but one great fact, and neglecting (as every person in such circumstances is more or less apt to do) whatever did not tend to support or overthrow his favourite hypothesis. A few of his experiments deserve particular attention,

By one, made on no less than 300 frogs, he has ascertained, that opium applied to a nerve does not affect the muscles in which it terminates,

It is foreign to the plan which, for the sake of brevity, I have adopted, to comment upon the inference that Fontana draws from this experiment, “*Que le*  
*“ vehicule de l’opium est la circulation*  
*“ du sang et des humeurs dans l’animal :*  
*“ et que sans elle l’opium n’exerceroit*  
*“ aucune action sur corps vivant.”* It is  
 directly



directly contradicted by almost innumerable observations.

The following experiment of Fontana's is one of more consequence. It was alluded to when speaking of Dr. Whytt's treatise on opium. An experiment of this author suggested it to Fontana. "I made (says the latter) a little opening in the scull of a certain number of frogs, through which I destroyed the brain and spinal marrow with a long pin. By performing the experiment in this way, rather than by cutting off the head, the great flow of blood which takes place in decollation was prevented; and consequently, in making experiments, frogs, with the nervous system destroyed in this way, can be more readily compared with the entire animal. Having then (he continues) made a certain number of  
frogs,

frogs, thus prepared, swallow each a certain quantity of opium, and the same number of entire frogs swallow each the same quantity, I opened the thorax in all of them, in order to observe the motion of the heart. I observed its duration, and from time to time stimulated the crural nerves, both in the one set of frogs and in the other; and I can assert, that having used in this experiment 48 frogs, 24 with the brain and spinal marrow, destroyed as above mentioned, and 24 entire, I could not perceive, that the opium produced a less effect, or operated more slowly, on the one set of frogs than it did on the other.

“ Je deduis cependant, de ces résultats, (Fontana continues), deux corollaires très importants : Le premier est, que le mouvement du cœur ne dépend  
 “ point

“ point des nerfs, ni de cet ensemble de  
“ sensations qui constitue la vie de l’ani-  
“ mal. Le second est, que l’action de  
“ l’opium l’exerce independamment du  
“ systeme nerveux.”

The former of these inferences is made from other experiments. It is plain, that the latter is not warranted by that just related. The only conclusion we can draw from it, and one indeed which it is impossible for us not to draw from it, is, that the motion of the heart is not affected by opium, applied to a distant part of the body, through the medium of the nervous system.

It is easy to count the beats of the heart, but impossible to determine accurately the state of the muscles, by irritating the nerves which terminate in them.

This

This part of the experiment lies open to much fallacy ; and that Fontana was deceived in the inference which he draws from it, appears from many facts related in the subsequent part of this paper.

Fontana found, in another experiment made on 24 frogs, that opium, thrown into the stomach, more speedily impairs the motion of the limbs in the entire animal, than in one with the heart cut out.

Dr. Alexander published his thesis, entitled, “ *De partibus corporis animalis. quæ viribus opii parent,*” at Edinburgh, in 1790. He attempts to show, (contrary to what seems ascertained by several of Dr. Monro’s experiments), that opium is never received into the system by means of the absorbents.

I think



I think it necessary to mention this attempt, because Dr. Alexander's experiments have been made since the publication of Dr. Monro's. But how unsuccessful it is, must appear at first view to every person who peruses the thesis.

No body can compare together the 52d, 54th, and 56th experiments, and read the comment which in the 106th and 107th pages the author makes upon them, without some surprize at seeing a man of Dr. Alexander's ingenuity permit himself to be so evidently misled.

Can it be seriously asserted, that because a frog with the spinal marrow divided, and 30 drops of a solution of opium applied to the extremities, survived another whose heart was cut out, and to whose extremities the same quantity

tity

tity of the same solution was applied : Can it be asserted, I say, from this experiment, that none of the effects of opium depend upon its absorption ? Is not cutting out the heart more suddenly fatal than the division of the spinal marrow ? and shall we make no allowance for this circumstance in drawing our conclusions from the experiment ?

Nor are his 59th and 60th experiments conclusive \*, since opium, applied to the inferior extremities, operates very slowly  
on

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\* Neither is Dr. Alexander's 51st experiment conclusive. The powers of absorption were probably deranged by the injury done to the part of the intestines on which the experiment was made. Besides, it was no easy matter to determine whether or not the lacteals contained a small quantity of the opium.

on the system in general ; and the injury done to the frogs in these experiments, previous to the application of the opium, was very considerable \*.

From some of Dr. Alexander's experiments it appears, that universal convulsions are the consequence of throwing a solution of opium into the stomach and intestines of a frog, although the heart has been previously removed. It was formerly observed, that Dr. Monro met with the same result, on injecting a solution of opium into the cavity of the abdomen, after cutting out the heart ; but he speaks as if he did not meet with this

C result

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\* Dr. Alexander was led, from his experiments on this head, to conclude, upon the whole, that although we cannot positively assert that opium is not absorbed, yet we have no proof of its being so, at least to such a degree as to kill.

result when the solution was thrown into the stomach and intestines.

Dr. Alexander shews, by many experiments, that opium, injected into the heart of a frog ; or into the stomach and intestines, or under the skin, whether the heart has been previously removed or not ; destroys the irritability of all the muscles of voluntary motion : but that it only produces the same effect on the muscles of involuntary motion when immediately applied to them.

He has also shewn, that if the nerves going to any limb be cut, the irritability of that limb remains after death, when the animal is killed by opium, in whatever manner applied, provided it has not been applied to the muscles of the limb itself.

As



As most of Dr. Alexander's experiments were made with a view to support or overturn certain hypothetical opinions, and as no inferences of consequence, except those relating to such opinions, can be drawn from them, few of this author's useful observations fall to be related here.

The last fact mentioned from Dr. Alexander's treatise is farther confirmed by Dr. Fowler, in a publication above alluded to, who used, as a test of the irritability of the muscles, the influence lately discovered by Galvani.

It may not be useless to present, at one view, the most important facts which have been stated.

Opium, applied to any part of a living animal, soon produces an aversion to mo-



tion, and a tendency to sleep. These effects often take place instantly when the dose is considerable, especially if it has been applied to a sensible part of the body \*.

If the dose is sufficient to endanger life, convulsions soon succeed, which consist of repeated contractions and relaxations of all the muscles of voluntary motion †. In different cases the contractions are more or less permanent.

Throwing a solution of opium into the blood-vessels produces the same effects as applying it in any other manner. A small quantity may be given in this, as in every other way, without occasioning  
either

\* Dr. Mead.

† Dr. Mead, Dr. Alston, Dr. Tralles, &c.

either convulsions or death \*. Convulsions are the consequence of throwing a strong solution of opium into the heart of a frog, whether the venæ cavæ and aorta have been previously divided or not †. The same solution thrown into the stomach and intestines, or into the cavity of the abdomen, after the heart is cut out, produces the same effect ‡.

After the brain and spinal marrow of a frog have been destroyed, without much loss of blood, a solution of opium, thrown into the stomach and intestines, affects the motion of the heart as readily as when the nervous system remains entire ||. Opium, therefore, applied to a

C 3

distant

\* Dr. Alston, Fontana, and Dr. Alexander.

† Dr. Monro.

‡ Dr. Monro and Dr. Alexander.

|| Fontana.

distant part, affects the motion of this organ through some other medium than that of the nervous system.

After all connection, by means of the nerves, between the hinder-limbs and trunk of a frog, is cut off, a solution of opium applied to these limbs produces the same effects on the body in general, as when their connection with the trunk is entire. From which we conclude, that opium is received into the system by means of the absorbents\*.

On throwing a strong solution of opium into the heart, it instantly becomes paralytic; nor can its action be renewed by any irritation whatever\*.

The

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\* Dr. Monro.

The application of this solution to the muscles of the extremities produces the same effect on them. But if every thing forming the connection between these and the trunk, except the nerves, be divided, its action extends no farther\*.

Thrown into the heart of a frog ; or into the stomach and intestines, or under the skin, either before or after the heart is removed ; it destroys the irritability of all the muscles of voluntary motion †.

Thrown into the cavity of the abdomen, it very suddenly renders the contractions of the heart less frequent ‡, and produces all its other effects more speedily than when injected into the stomach.

\* Dr. Monro.

† Dr. Monroe.

† Dr. Alexander.



mach and intestines, or merely applied to the abdominal muscles \*.

Lastly, it operates most speedily on those animals which cannot live long without a fresh supply of food and air †.

Such may be considered the present state of our knowledge concerning the action of opium on the living animal body.

On reviewing what has been said, we still find the subject involved in much confusion.

Opium, it has been observed, so affects the nerves of the abdomen, stomach, and  
intestines,

\* Dr. Whytt and Dr. Monro.

† Dr. Whytt.

intestines, and those of the heart, as to act by what has been termed the Sympathy of Nerves, on every, the most distant part of the body, after the circulation is interrupted ; and yet no action of opium on the nerves of the extremities produces the same effect. And altho' a solution of opium, directly applied to the heart, thus affects distant parts of the body, and the motion of this organ is almost immediately influenced by injecting the solution into the cavity of the abdomen, *i. e.* far more speedily than it could be through the medium of the absorbents ; yet throwing a large quantity of opium, into the stomach and intestines, does not affect the motion of the heart, through the medium of the nervous system.

These circumstances very nearly imply contradictions, and certainly do not tend  
to

to establish any general laws concerning the action of opium on living animals.

My reason for laying the following experiments before the public is, that they contradict many of the most essential of the above-mentioned circumstances, at present regarded as incontestible facts; that they remove the seeming contradictions just stated; and that they seem to afford a very simple account of the *modus operandi* of opium on living animals; that is, to shew on what parts of the system this drug immediately acts in producing each of its effects, and that its action on these parts does not essentially differ from that of a vast number of other substances.

But I do not assert, that because they  
remove

remove these seeming contradictions, and afford a more simple account of the *modus operandi* of opium than those which have been related or alluded to ; I am very far (I say) from asserting, that on these accounts their results ought to be granted ; especially when they contradict the inferences which we must draw from the experiments of a Whytt, a Monro, or a Fontana.

The only means of arriving at certainty in experiments, where there is so much room for fallacy as in those I am speaking of, is frequently repeating them ; and although the circumstances just mentioned tend doubtless to confirm the results of the following experiments, it is solely on this ground that I bring them forward, namely, that they have been  
much



much more frequently repeated than those, from which opposite conclusions must be drawn.

*EXPE-*

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*EXPERIMENTS, made with a view to determine the manner in which Opium acts on the Living Animal Body.*

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I BEGUN these Experiments by repeating the most simple of those which had been made by others. Opium was applied to various parts of the entire animal, both external and internal, and the results found precisely such as various authors have stated them.

The animal constantly became affected  
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with violent and univerfal fpafms, which almoft immediately followed the exhibition of the opium, when it was applied to the brain, or injected into the heart and blood-veffels.

After making many experiments which led to no ufeul conclufion, any account of which, therefore, would be improper, the following obfervation fuggested feveral of thofe, I am about to relate.

On throwing a folution of opium into the heart, I thought I perceived it pafs along the aorta towards the brain. Comparing this circumftance with the effects of opium applied to that organ, it appeared probable, that the convulfions which follow its injection into the heart and blood-veffels, are owing, not to any  
 fympathy

sympathy of the nerves of the heart with those of other parts of the body, but to the opium being conveyed through the aorta, and immediately applied to the brain. With a view to determine this point, I made the following experiments.

The solution used in the first and many of the other experiments, was prepared in the following manner. One ounce of opium was triturated with two ounces of warm water, till a turbid mixture was formed: one ounce of cold water was afterwards added to it. This mixture was carefully corked, and exposed to a temperature of  $90^{\circ}$ \* for 12 days. It was  
then

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\* Of Farenheit's thermometer.



then filtered, and about two ounces and a half of a very strong solution obtained, which appeared almost black in a common two-ounce vial. This solution is stronger than that which was used either by Dr. Monro or Dr. Alexander. A weaker was prepared by mixing equal parts of this solution and water \*.

After securing the aorta by ligature in 12 frogs of different sizes, a few drops of the strong solution of opium was injected into the heart of each. It immediately ceased moving. This, however, was not followed by the slightest convulsion in any part of the body.

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\* In many of the following experiments, it is of no consequence to know the strength of the solution employed: it is not therefore attended to in these.

The frogs all died in exactly the same manner as these animals do when the heart is cut out; that is, when the circulation is interrupted, and when they lose as much blood as in this experiment. I could not perceive that the injection of the solution had any effect, but that of putting a stop to the motion of the heart.

The irritability of the muscles of voluntary motion, after death, was found, in all of these frogs, as entire as it is after any death equally lingering.

A similar experiment was made in the following manner: After dividing the aorta in ten frogs, most of them full grown, a few drops of a solution of opium, (not quite so strong as that used in the last experiment), were thrown into the

D heart

heart of each. Its contractions instantly ceased, but no convulsions supervened.

I have neglected, I find, to mention in my notes the degree of irritability remaining, after death, in the muscles of these frogs. I seldom or never failed to examine it, however, and I recollect, that in all experiments of this kind, that is, in which a solution of opium was injected into the heart, after dividing the aorta, or securing it by ligature, the muscles of voluntary motion were readily thrown into contractions, after death, by irritating the nerves which terminate in them.

A circumstance which occurred in making this experiment, serves, in some measure, to account for others having met with a different result from it. Having divided the aorta, as I imagined,



and injected some drops of the solution into the heart of a frog, I was surprised to observe, (contrary to what happened in the experiment just related), the animal seized with universal convulsions.

On examining the part of the aorta, however, at which the cut had been made, the cause of this difference of result appeared very evident. I had not completely divided the artery, the two ends still adhered by a slight connection on the inner side of the vessel; and as the elasticity of its sides preserved its cavity, any fluid injected into the heart must in part have passed along this vessel to the brain. The consequence would have been the same, it is evident, had the cut ends of the vessel been kept applied,



or nearly so, by cellular membrane, or any other means.

I accidentally observed, in more than one instance, that convulsions did not supervene, when the solution was injected into the heart in very small quantity, and with very little force, although the aorta was neither divided nor secured by ligature. This mode of making the experiment is certainly more conclusive than either of the foregoing; since many of the nerves of the heart pass so near the aorta, that they must share its fate, when we divide or throw a ligature around this vessel.

But it is almost impossible to repeat the experiment frequently in this way with the same result. It is difficult to inject the solution in such a manner, that no part

of it may pass into the aorta, or always to determine whether it does so or not \*.

This, however, suggested another mode of making the experiment, which seems perfectly conclusive.

I slit the heart in fix frogs. Notwithstanding its contents were thus instantly  
D 3                      evacuated,

\* This mode of making the experiment, although its result is not always uniform, ought perhaps to be regarded as sufficiently conclusive. When convulsions follow the injection of the solution, we can readily account for their doing so, independent of any action of the opium on the nerves of the heart. And when they do not, how are those, who attribute these convulsions to what is termed sympathy of the nerves, to account for their absence, when the solution is injected into the heart, while the nerves of that organ, and those of every other part of the system, remain entire?

evacuated, it continued to contract with vigour. A little of the same solution used in the last experiment was then dropped into it.

No part of the solution, applied in this way, can be sent through the arteries to the brain; but as all the nerves are left entire and uncompressed, if the convulsions which follow the injection of opium into the heart depend on any action of that drug on the nervous system, they ought to be observed in this experiment.

On dropping the solution into the heart, it immediately ceased moving, but no convulsions supervened.

Left it should be said, that putting a stop to the circulation in the above experiments,

riments, prevented the nervous system from undergoing the changes necessary for producing convulsions, the following was made.

The aorta in four frogs was secured by ligature, and the auricle wounded so as to permit the blood to escape ; in other two, a ligature was thrown around all the vessels attached to the heart ; and this organ was removed. The skull of each was then perforated ; and, after wounding the brain in the first four, a little of the weaker solution was dropped into it. In the other two, a few drops of a stronger solution were applied to the surface of the brain.

In all of them the muscles of voluntary motion were seized with the most violent convulsions. They died, with



precisely the same symptoms which follow the injection of opium into the heart, when it passes along the aorta.

On examining the state of the muscles after death, in the first four frogs, their irritability was found much impaired. I either did not examine the state of the muscles, after death, in the other two frogs, on which the experiment was made at a different time, or neglected to take notice of it in my notes.

The frogs used in this experiment were of different sizes; two of the first four were full grown.

From these experiments, then, it appears, that opium, applied to the heart, is not capable of affecting any distant part,  
through

through the medium of the nervous system.

Another perplexity, however, relating to the action of opium on the heart, still remains to be unravelled.

Dr. Monro, it has been observed, found, that, by throwing a solution of opium into the cavity of the abdomen of a frog, the motion of the heart is almost immediately rendered less frequent ; from which this author concluded, and certainly not without reason, that opium, applied to a distant part of the body, affects the motion of the heart through the medium of the nervous system.

As this conclusion, however, contradicts the result of an experiment of Fontana's, above related, which was repeated  
much

much more frequently than Dr. Monro's, I suspected that there had been some fallacy in the latter.

I therefore repeated Dr. Monro's experiment more than once, but found the result as he has stated it. The beating of the heart became less frequent, almost immediately on injecting the solution into the cavity of the abdomen.

It was still plain, however, that both the conclusion which has been drawn from this experiment, and that which Fontana draws from his, could not be just, as they directly contradict each other.

There seemed little doubt of the justness of Fontana's conclusion. That of the other appeared more questionable. In the former,  
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mer, it is only maintained, that a certain effect is not produced by the opium, because it is not observed to follow its exhibition; in the latter, it is not only maintained, that the opium produces a certain effect constantly observed to follow its exhibition, (an inference indeed as just as the other); but that it produces this effect in a particular way.

These circumstances led me to consider, whether or not there is any other way, in which a solution of opium, injected into the cavity of the abdomen, can be supposed to influence the motion of the heart, besides through the medium of the nervous system, or that of the absorbents.

A conjecture occurred to me, which is  
confirmed



confirmed by several of the following experiments, namely, that opium applied to the coats of the blood-vessels, by destroying their muscular power, (opium, it was found, destroys the power of action in all muscles to which it is immediately applied), must affect the circulation in these vessels; and consequently, thrown into the cavity of the abdomen, influence the motion of the heart, by impeding, or entirely interrupting, that of the blood, in nearly one third of the whole animal; by which the supply to the heart is diminished, and a greater than usual obstacle opposed to its perfect evacuation.

The first circumstance, then, to be ascertained, is, whether opium applied immediately, or nearly so, to the blood-vessels of a living animal, impedes, or wholly interrupts,

interrupts, the circulation in these vessels, independent of any general affection of the system.

It is to be observed, that in the following experiment, the opium is not applied immediately to the coats of the blood-vessels, but injected into a cavity, between which and these vessels a dense membrane of cellular substance is interposed. The skin of a frog, except in a few places, (chiefly the joints), does not adhere to the parts which lie beneath it.

Having adapted the web of a frog's foot to a microscope, I injected eight or ten drops of a solution, (nearly as strong as the stronger solution), under the skin of the leg.

In a few seconds the circulation became

came languid, and no motion could be perceived in some of the larger blood-vessels. It gradually became more obscure in the rest, till, in the space of about two or three minutes after the injection of the opium, it ceased altogether. Nor did this interruption of the circulation proceed from any general affection of the system, since the motion of the blood still continued in the other foot.

Left it might be suspected that in applying the foot to the instrument, the vessels were compressed, it is proper to observe, that the circulation in the foot after it was applied to the microscope, continued as vigorous as natural, till the solution was injected. On another occasion, indeed, I have observed, the circulation in the foot of a frog, applied



plied in the same way to the same microscope, vigorous for several hours.

This experiment was made three times, in the same manner, and with the same result.

After determining that opium is capable of interrupting the circulation in the part to which it is immediately applied, independent of any general affection of the system; all that is necessary in order to ascertain whether it is in this way that it suddenly affects the motion of the heart, when thrown into the cavity of the abdomen, is to interrupt the circulation, and observe the effects of this drug applied in the same way, when it can only act on distant parts, through the medium of the nervous system.

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The functions of this system, it has already been observed, are not impaired in the frog, for a considerable time after the circulation is interrupted \*.

I slit the heart in six frogs, so as to permit the blood to escape freely ; and in about a minute after, threw eight or ten drops

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\* It may seem that I should, in the first place, have shewn, that diminishing the quantity of blood, supplied to the heart, is capable of diminishing the frequency of its contractions. An experiment of this kind is perhaps unnecessary, as the fact which it goes to prove is so generally admitted. But, that nothing may seem taken for granted, it will be found in the following experiment, that, after the ventricle of the heart was wounded, and thus a great part of the blood evacuated, the struggles of the animal, which increased the flow of blood to the heart, never failed at the same time to increase the frequency of its contractions.

drops of the same solution, used in the last experiment, into the cavity of the abdomen, moving the tube, with which the injection was made, in various directions, that the solution might be applied as generally as possible. Little or none was returned.

In three of the frogs, the frequency of the heart's motion was the same after as before the injection of the solution ; in the other three, it became less frequent about a minute after it.

There is room for considerable fallacy in this experiment. Cutting the heart may render its contractions more frequent than natural, and consequently their frequency will diminish more rapidly than when the heart is left entire. Besides, I always observed, that the struggles of the animal, increasing the supply

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of blood to the heart, increased the frequency of its contractions; and as this supply was always becoming less, their frequency, on this account also, would be constantly diminishing. It is extremely probable, that the diminished frequency of the heart's motion, in three of the frogs, was not the effect of the opium, since it did not produce the same effect in the other three.

As it is possible, however, that some unperceived circumstances might have counteracted the effects of the opium on the first three frogs, it was necessary to repeat the experiment in a more conclusive manner.

I observed, that although, on securing the aorta by ligature, the heart is immediately distended with blood to a great degree, the frequency with which it beats

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after



after the operation, continues the same, or nearly so, for the space of four or five minutes. It is increased when the animal struggles; but there seemed no other circumstance to influence the result of the last experiment, performed in this way; and it was easy to make allowance for this.

After securing the aorta by ligature, therefore, in six frogs, and counting the beats of the heart, eight or ten, and in some fourteen or sixteen, drops of the same solution used in the last experiment, were injected into the cavity of the abdomen, the tube being moved in various directions, as formerly. Little or none was returned.

When the animal struggled, which most of them did the moment the injection was made, the frequency of the heart's



motion was for a little increased. With this exception, it continued, in all of them, to beat with the same frequency after as before the injection of the solution, for the space of four or five minutes; at the end of this time, it began to lose several beats in the minute; but this was the consequence of securing the aorta, as I found by securing this vessel in other three frogs, without injecting any of the solution \*.

The inference from these experiments is, that the diminished frequency of the heart's motion, observed almost immediately on throwing a solution of opium into the cavity of the abdomen, does not  
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\* The two latter experiments were made, because, in Fontana's above alluded to, the opium was applied only to the stomach and intestines, while, in Dr. Monro's, it was thrown into the cavity of the abdomen, which might appear to some, perhaps, sufficient to account for the difference of their results.

proceed from any action of the opium on this organ, through the medium of the nervous system, but from its impeding, or entirely interrupting, the circulation, in nearly one third of the whole animal.

Opium immediately applied, even to the brain itself, although it excites violent and universal convulsions in the muscles of voluntary motion, seems, from the following experiments, incapable of at all affecting the contractions of the heart.

I removed a piece of the cranium in two rabbits, about the size of a sixpence, and as much of the dura and pia mater as I could, without injuring the brain. After replacing the teguments, and joining the lips of the wound by a

future, about a drachm and a half of a solution of opium in water was injected under the skin. This mode of applying the opium to the brain I found very convenient ; it was suggested to me by a gentleman present when I made this experiment.

Soon after the injection of the opium, the animals were seized with violent convulsions. But the motion of the heart, which I examined from time to time, was not in the least affected, except that it became more frequent when the muscles of the limbs were alternately contracted and relaxed.

In the space of some hours, the animals were reduced to a state of great debility, the muscles of voluntary motion being affected with a degree of paralysis. But  
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the motion of the heart still continued strong and regular.

I thought I felt a slight irregularity in its motion in one of these rabbits, about an hour before its death, near twenty-four hours after the solution of opium was injected. This I could not again perceive, although I frequently examined the motion of the heart afterwards.

On opening the thorax of this rabbit, a few seconds after its death, I found the heart contracting regularly. The contractions of the ventricles continued for near ten minutes, gradually becoming less vigorous. Those of the auricles were seen for a much longer time.

This rabbit had been considerably debi-



litated the day before the experiment, by a quantity of opium thrown into its stomach.

The other was quite healthy, and had rather more of the solution applied to its brain. It died in nine hours.

The heart of this rabbit beat strongly, and with perfect regularity, both during the spasms, and subsequent paralysis of the limbs. It was at last seized with uncommonly strong convulsions, in which it almost instantly expired.

Immediately after its death, I applied my hand to the thorax, and felt the heart beating regularly for a few seconds. Its beats, when the hand was first applied, were little inferior in strength to those of the heart of a healthy rabbit. In the other,

the motion of the heart could not be perceived, after death, from the outside of the thorax.

It is a curious circumstance, that at the time, the animals used in this experiment were thrown into convulsions by the slightest touch, their sensibility was so much impaired, that on running a knife through the foot of one of them, it showed no signs of pain; only starting convulsively, as it did when touched with the finger.

After removing a part of the cranium, and laying open the thorax, in seven frogs, a little of a solution of opium was applied to the brain, the muscles of voluntary motion were soon seized with the most violent spasms; but the motion of the heart continued perfectly natural, except  
when

when disturbed by the convulsions of the trunk and limbs.

It has been observed, that, during the remissions of these convulsions, a very slight irritation is capable of renewing them. But on irritating the heart, even roughly, in this experiment, no irregular contractions could be excited in it.

Dr. Monro informed me, that he had, for some years past, performed the following experiment publicly in his Anatomical Theatre.

He injected a solution of opium in water, through a hole made in the cranium of a frog, in such a manner that it passed along the spinal marrow, and part of it came out at a hole made in the lower end  
of

of the spine. By this mode of applying the opium, the animal was instantly killed.

An experiment, in which the nervous system is so completely deranged by the action of opium, seemed well fitted for determining, whether this drug, applied to the brain and spinal marrow, is capable of directly influencing the motion of the heart. I therefore repeated the experiment in the following manner.

A hole was made in the cranium, and another in the lower end of the spine, in eight frogs ; a strong solution of opium, in water, was then injected through the hole made in the cranium, in such a manner that it passed along the spinal marrow, and part of it came out by the hole in the spine.

Most



Most of the frogs were deprived of sense and motion as soon as the solution was injected; in two or three it was necessary to repeat the injection before the same effect was produced on them; and although they all appeared for some time quite dead, in the space of two or three minutes most of them were seized with a trembling in the limbs, and some with strong spasms, which, during their intermissions, were not renewed by a slight irritation, as those are which follow the application of opium to the brain only. I observed, however, that when they had not previously taken place, they were often excited by laying open the thorax. This was done in all the frogs used in this experiment; and in those in whom it excited convulsions, or trembling, as well as in those in which no motion whatever

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in the muscles of the trunk or limbs took place, after the injection of the solution, the motion of the heart was found as vigorous as it is in healthy frogs \*.

The solution used in this experiment must be sufficiently strong to deprive the animal of motion, at least till the thorax  
is

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\* A gentleman, who was present when I was making this experiment, having prepared a frog in the above manner, injected the caustic volatile alkali instead of the solution of opium. This also instantly deprived the animal of sense and motion : he then laid open the thorax, and shewed me the heart uncommonly pale, and its motion considerably weaker than that of the heart in a healthy rabbit. I was inclined to attribute this affection of the heart, however, to the acrid vapour of the alkali, (in which the frog was immersed, and which affected the eyes violently while we were examining the animal), being applied to this organ as soon as the thorax was laid open. I therefore laid  
open

is laid open ; for I found in several other trials, that the uncommonly strong spasms induced on the limbs, when this is not the case, by rendering the circulation very irregular, and often, for some seconds, wholly interrupting it, greatly deranges the motion of the heart, by gorging it with blood ; and seldom fails, more or less, to impair its vigour. So that, what at first sight might seem a paradox, a small quantity of opium, applied

open the thorax of a healthy frog, and exposed its heart to the same vapour, which immediately produced on it precisely the same effects. We then repeated the above experiment in the following manner : Having injected the caustic volatile alkali as formerly, the animal was instantly deprived of sense and motion. It was then carefully washed, that the vapour of the alkali, after the thorax was laid open, might not be applied to the heart, which was now found as vigorous as that of a healthy frog.



plied in this way, enfeebles the motion of the heart, while a larger quantity is incapable of at all affecting it.

The following manner of making this experiment is perhaps more conclusive: After making a hole in the cranium, and another in the lower part of the spine, the thorax was laid open, and the motion of the heart carefully observed in seven frogs; the solution was then injected as formerly, by which the animals were instantly deprived of voluntary motion, and appeared quite dead; but the motion of the heart was not in the least affected; it continued with the same frequency and vigour, as before the injection of the solution.

All the frogs used in this experiment, some time after the injection of the solution,



lution, were seized with trembling, or convulsions, in the trunk and extremities.

I may observe, by the bye, that although irritating the brain mechanically, (like the application of opium to this organ), produces violent and universal convulsions in the muscles of voluntary motion, both in frogs and rabbits; yet I have found, that in neither the one nor the other it affects the motion of the heart \*. It would be digressing too far to consider fully the inferences which these and many similar observations seem to warrant.

It is sufficient, in the mean time, to observe, that from the experiments  
which

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\* Fontana makes the same observation respecting frogs.

which have been related, we arrive at this conclusion, that opium, applied to a distant part of the body, does not affect the motion of the heart, through the medium of the nervous system; nor, on the other hand, does opium, applied to the heart, affect any other part of the body, through the same medium.

But the heart is not the only muscle which opium, applied to a distant part, seems incapable of affecting, through the medium of the nervous system.

Many considerations render it highly probable, that the same is true of all the muscles of involuntary motion, without exception. That it is so of the muscular coat of the alimentary canal, which, next to the heart, may be considered the

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chief

chief of this class of muscles, appears from the following experiment.

The abdomen in several healthy rabbits was laid open, and the peristaltic motion of the intestines, which became very considerable a few seconds after they were exposed to the air, carefully observed.

A large portion of the cranium was removed in another rabbit, and the brain cut across its whole depth, in three directions. A small part of it also, which, after the cuts were made, projected beyond the edges of the bone, was removed. A solution of opium in water was then injected into the brain, by means of a small tube passed in various directions through its substance.

This was immediately followed by the  
most

most violent and universal convulsions of the muscles of voluntary motion, which, in the space of a minute or two, became quite rigid, and as hard as a piece of board. The animal lay with its head drawn back, its limbs extended, in short, affected with violent and complete tetanus.

In this situation, its abdomen was laid open, and the peristaltic motion of the intestines found, in all respects, similar to that observed in the other rabbits used in this experiment. I could not perceive that it was stronger or weaker, more or less irregular, in the one case than in the other.

On examining this rabbit, twenty-five minutes after the solution was injected into its brain, the muscles of voluntary



motion were found quite flaccid, and the animal dead. The motion of the intestines, however, was still strong in many parts of their tract, and continued so for thirty-six minutes longer, during which time I observed it. It was not again examined till forty-four minutes afterwards; the intestines were then cold and motionless.

In making this experiment, it is to be observed, that handling the intestines throws them into violent spasms, whether opium be applied to the brain or not; and that those parts which are most exposed to the air lose their motion soonest: so that it is necessary to raise these, and examine the parts which lie beneath them, if we wish to ascertain how long the peristaltic motion continues.

This

This motion, I may observe, like that of the heart, is not in the least affected by mechanically irritating the brain. In making this experiment, the animal must be well secured, otherwise the violent convulsions, induced on the muscles of the limbs by tossing the intestines, will increase the peristaltic motion.

It has been shewn, that opium, applied to the external surface of the heart, very little, if at all, affects the muscular power of this organ; applied, in considerable quantity, to its internal surface, it immediately destroys it. In like manner, applied to the external surface of the intestines, I could not be certain that it all diminished the peristaltic motion: on injecting it into their cavi-

ty, they almost instantly became paralytic \*.

On comparing the experiments which have been related, particularly the first related, with those in which opium thrown into the stomach and intestines, cavity of the abdomen, &c. is found to produce convulsions, it appeared probable, that in the latter cases, as in the former, the convulsions do not proceed from any action of the opium on the nerves of the part to which we apply it, but from its being received into the sanguiferous system, and immediately applied to the brain.

And

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\* From this effect of opium on the internal surface of the intestines, we are at no loss to account for the costiveness which attends the use of this drug.

And this conjecture appeared the more probable, as the convulsions do not supervene for a considerable time after the exhibition of the opium, except when it is thrown into the sanguiferous system, or applied to the brain itself. In order to determine this point, and at the same time what effect opium produces, merely by its action on the nerves of the part to which it is applied, (if universal convulsions of the muscles of voluntary motion be not this effect), I made the following experiments.

It has more than once been observed, that the nervous system of the frog is capable of performing all its functions for a considerable time after the circulation is interrupted. A full-grown frog leaps about vigorously, for half an hour after the heart is cut out, by which not



only the circulation is interrupted, but the greater part of the blood evacuated : And it generally continues to leap, when irritated, for more than twice that time.

All that was necessary, therefore, to determine the point in question, was to cut out the heart, or otherwise interrupt the circulation, and then observe the effects of opium applied to the stomach and intestines, or injected into the cavity of the abdomen.

This experiment has been made, it was observed, by more than one author, and the result was general convulsions of the trunk and limbs.

As some unperceived circumstance, however, might have influenced the result of these experiments, such as, a small  
 2 quantity

quantity of the solution of opium having been accidentally applied to the skin, before the heart was removed, (see the 2d experiment with tobacco, at the end of this paper), as the experiments were made on but a small number of frogs; and as those who made them do not altogether agree concerning the part to which the solution must be applied, in order to induce convulsions, after the heart is removed, I thought it worth while to repeat the experiment on a larger scale.

After cutting out the hearts of 24 frogs, a solution of opium in water was injected into the stomach and intestines of some of them, and into the cavity of the abdomen of others. The following are the particulars relating to each. The strong

strong solution was used, except when the contrary is mentioned.

Into the 1st, not full grown, 30 drops were injected ; it died in half an hour : Into the 2d, not full grown, the same quantity ; it died in 35 minutes : Into the 3d, the same quantity ; it died in 51 minutes : Into the 4th, very young, 10 drops ; it died in 25 minutes : Into the 5th, almost full grown, 30 drops ; it died in an hour : Into the 6th, full grown, 30 drops ; it died in 55 minutes : Into the 7th, full grown, 60 drops ; it died in an hour and two minutes : Into the 8th, full grown, 60 drops also ; 8 or 10 were returned ; it died in 58 minutes : Into the 9th, not quite full grown, 30 drops of the weaker solution ; the time of its death was not observed : Into the 10th, very young, 10 drops of the weaker  
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er solution ; it died in 54 minutes : Into the 11th, not full grown, 50 drops of the same solution ; part was returned ; the time of this frog's death was not observed : Into the 12th, very young, 10 drops of the same solution ; part was returned ; the time of its death was not observed : Into the 13th, not full grown, 26 drops of the same solution ; it died in 59 minutes : Into the 14th, nearly full grown, 63 drops of the same solution ; part was returned ; it died in 52 minutes : Into the 15th, 20 drops of a solution nearly as strong as the strong solution : Into the 16th, 15 drops of the same solution ; about 3 were returned ; the time of the death of neither of the two last frogs was observed.

Solutions of various strengths were injected into the eight remaining frogs ; in-  
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to some a weaker, into others a stronger solution, than that employed in any of the above cases.

Those which were of the same size, generally died the sooner, the greater the quantity of opium which had been injected. Young frogs die much more readily from injuries of this kind, than those which are full grown, as may be seen from several parts of this experiment.

The manner in which all these frogs died was precisely the same: Soon after the injection of the opium, they were seized with a degree of langour, generally proportioned to the quantity injected. This, in most of them, went off to a greater or less degree, in the space of some minutes. They again, more gradually,

dually, became languid, and growing more and more so, imperceptibly died, without the slightest convulsion in any part of the body. I neglected to examine the state of the muscles, after death, in the fourth frog used in this experiment; in all the others, they were found to contract readily, on wounding the nerves which terminate in them.

Fifty drops of a very strong solution of opium in water, considerably stronger than the strong solution, was injected into the cavity of the abdomen, of one of the last eight frogs, full grown, the heart, as in the other cases, having been previously cut out. Part of the solution was returned when the animal moved.

For a few seconds after the injection of the solution, it leaped about with vigour ;

gour ; in a short time, however, it seemed incapable of leaping ; and in the space of two minutes, was almost quite deprived of motion. It soon began to move again, and in eight minutes could leap about. Fifty-one minutes after the injection of the solution, it leaped on being much irritated. Twenty-eight minutes after this, it turned itself when laid on its back. It died in about an hour and twenty-eight minutes after the injection of the solution.

I have related this instance particularly, as it is remarkable for the great degree of langour which followed the injection of the opium, and for the length of time which the animal, notwithstanding this, survived the application of that drug.



The foregoing experiment was repeated in the following manner. The thorax was laid open in eight frogs, and a ligature thrown around all the vessels attached to the heart : This organ was then removed, with the loss of no more blood than it happened to contain at the time the ligature was thrown around the vessels. A solution of opium was then injected into the cavity of the abdomen in all of them, through a hole made in the muscles.

The solution injected into the first 6, was not quite so strong as the strong solution ; that injected into the 7th and 8th, was stronger. All the frogs used in this experiment, except the 6th, were full grown. Into the 1st, 16 drops were injected : Into the 2d, 20 drops ; about 2 or 3 of which were returned : Into the  
3d,



3d, 16 drops; about 3 were returned : Into the 4th, 25 drops; about half was returned : Into the 5th, 8 drops : Into the 6th, 30 drops; part of which was returned : Into the 7th, 12 drops; part was returned : Into the 8th, 14 drops.

The frogs used in this experiment died in precisely the same manner as those used in the last. The muscles of their limbs contracted readily after death, when the nerves terminating in them were irritated.

It appears from these experiments, that the effect of opium, when it acts on the nerves of the part to which it is applied, is merely that of inducing a general languor, which, if the quantity applied be considerable, terminates in death. This effect of opium does not essentially differ from

from that of any other topical irritation\*.

From all that has been said, it appears, that the various effects of opium on the living animal body may be divided into three classes. The first, comprehending its action on the nerves of the part to which it is applied, not differing essentially

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tially

\* In man it has been shewn, that a large dose of opium produces sleep, merely by its action on the nerves of the part to which it is applied ; so do other topical irritations (mechanical injury not excepted), though more slowly. If it be this effect of opium which Dr. Whytt alludes to, when he says, that opium destroys the power of motion in every part of a frog, as speedily after as before the excision of the heart, the observation is certainly just. From the nature of the experiments from which he draws the conclusion, however, he does not seem to allude to this effect of it.

tially from that of any other topical irritation. It is doubtful whether the shock given to the system, merely by the action of opium on the nerves of the part to which it is applied, has ever been sufficient to kill. I have never seen it produce so remarkable an effect in any other case as in one above related.

A large quantity suddenly applied to a very extensive surface, may be capable, perhaps, of instantly killing animals less tenacious of life than frogs are. A variety of strong impressions, that produced by receiving a large quantity of spirit of wine into the stomach, of very cold water when the body is overheated, &c. are well known to have occasioned sudden death. It seems to be a general law of the animal œconomy, that the first effects of a strong irritation  
are

are very violent ; but if these be withstood, it is afterwards borne with less inconvenience. It has just been shewn, how strikingly true this is of the effects of opium, when it acts only on the nerves of the part to which it is applied.

The second class into which the effects of opium may be divided are, its effects on the heart and blood-vessels ; that of increasing their action, when applied in small quantity \* ; and that of impairing

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or

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\* It has been observed, that a short time after we take a moderate dose of opium, the pulse becomes quicker and fuller ; an effect, which, from the experiments that have been related, can only proceed from the opium being absorbed and immediately applied to the heart ; since it has been proved, that opium cannot affect the motion of this organ through the medium of the nervous system.



or altogether destroying their power of action, when applied to them more freely \*. In neither of these effects, however, does the action of opium differ essentially from that of many other substances. Are not most acrid substances, in small quantity, capable of exciting strong contractions in the muscular fibre, and of destroying its power of action, when applied more freely †? Even mechanical

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\* It does not appear, that, by the largest dose, we can so increase the quantity of opium absorbed, that it is sufficient to destroy the muscular power of the heart, merely by its action on that organ. It may be safely asserted, perhaps, that opium never kills by destroying the muscular power of the heart, except when injected into it, or into the blood-vessels.

† But the tendency of different substances to increase or destroy the action of the muscular fibre is different

chanical irritation, applied in different degrees, produces the same effects.

The third class, into which the effects of opium may be divided, comprehends those it produces when immediately applied to the brain. When the dose is moderate, impaired sensibility, langour, sleep: Effects observed in a greater or less degree, from other gentle irritations applied to this organ, and which we do not perceive from a moderate dose of opium, till we know from the symptoms it produces, compared with the foregoing experiments, that it has been conveyed to the heart; from which, in the course of circulation, it is sent to the brain, as

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well

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different. Tobacco, for instance, is more apt to destroy, and less apt to increase, its action, than opium.

well as to the other parts of the body. What share its action on the latter parts has in producing these effects, it is impossible to say. We have reason to believe it but trifling. It appears from the experiments just related, that no part of them is to be ascribed to its action on the heart itself\*.

Opium, applied more freely to the brain, produces the same effects which most violent irritations, immediately applied to this organ do, convulsions and death

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\* The increased determination of blood to the head indeed, in consequence of the stronger action of the heart, is found to dispose to sleep; but this, in the present case, may be overlooked, as the effects of the opium applied to the brain are so much more considerable.

death \*. But the convulsions produced by opium, it has been shewn, are of a peculiar kind. In each of its effects on the living animal, we still find that opium has much in common with other substances, but, at the same time, something peculiar to itself.

It may appear an omission, not ranking among the effects of opium received into the system, those it seems to produce on the muscles of voluntary motion. In some of the foregoing experiments, the irritability of these muscles was found much impaired after death ; although the opium was not applied directly

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rectly

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\* Opium does not always prove fatal, when it produces convulsions. I have seen a rabbit recover after violent convulsions induced by a large dose of this drug.



rectly to the muscles themselves. The reason of this seeming omission will appear from the following observations.

Comparing Fontana's experiment (in which he found the irritability of the muscles as little impaired by the action of opium applied to the stomach and intestines of the entire animal, as to those of one with the heart cut out), with others which have been related, we should infer, that the presence of opium in the system scarcely, if at all, affects the irritability of the muscles of voluntary motion. From Dr. Alexander's experiments, on the other hand, we must conclude, that they are wholly deprived of their irritability by that drug, whether it be received into the system by means of the absorbents, or act merely on the nerves  
of

of the part to which it is directly applied.

Were I to trust to the accuracy of my own observations, I should dissent from both opinions. I have never found the irritability of these muscles wholly exhausted by opium, applied in any manner, except to the muscles themselves. Nor have I found their irritability as little affected by the application of opium to the stomach and intestines of the entire animal, as to those of one with the heart cut out.

Upon the whole, the result of my experiments on this part of the subject has been, that if opium occasions convulsions, it impairs the irritability of the muscles of voluntary motion; if it does not,  
their

their irritability is not in the least affected by it.

From which it appears probable, that the impaired irritability of these muscles, observed in the former case, is the consequence of the violent contractions excited in them by the irritation applied to the brain, and not of any action of the opium on the muscles themselves. In order to determine the truth or fallacy of this opinion, I made the following experiment.

After injecting either into the stomach and intestines, or into the cavity of the abdomen, I forget which, (for I have lost the notes of this experiment), of two frogs, equal in size and vigour, the same quantity of opium; the one was kept free of every thing which, during the remission

mission of the convulsions, might tend to renew them; so that they were rendered as moderate, and the remissions as long, as possible; in the other, as soon as a remission took place, the convulsions were renewed by slightly touching it; so that, although both frogs had taken the same quantity of opium, yet the one was affected with more violent and permanent convulsions than the other.

If, then, the impaired irritability of the muscles of voluntary motion, observed after death, when an animal is killed by opium, depends on the presence of this drug in the system, the state of these muscles in both the frogs used in this experiment should be found the same. If it be the consequence of the contractions excited in the muscles, it should be



more observable in the one frog than in the other.

The latter was found to be the case, in a very remarkable degree. I do not exactly remember how often this experiment was repeated; but recollect that it was not made above two or three times; so that its result can scarcely be regarded as certain. Some other experiments have been related, however, which tend to prove the same thing.

It was observed, that both Dr. Alexander and Dr. Fowler have shewn, that if the nerves going to any limb be divided before the solution of opium is exhibited, the muscles of this limb are neither affected with convulsions previous to death, nor is their irritability found impaired after it. Yet the opium is conveyed

veyed to them, in the course of circulation, as well as to those of any other part of the body.

The test of the degree of irritability remaining in the muscles after death, which was used in the foregoing experiments, is doubtless a very gross one. A nice test in these experiments would have been of little consequence, however ; since the irritability seems affected by circumstances so various, that, without an infinite number of experiments, we could not ascertain to what the small differences, detected by such a test, are owing.

The influence, discovered by Galvani, appears at first sight an excellent test of the degree of irritability remaining in muscles, and has been used as such ; but  
its

its laws seem at present too little known to permit us to employ it with much confidence in physiological inquiries.

I am inclined to believe, that a certain state of the nerves may prevent this influence producing contractions in muscles, even while their irritability remains; at least I found, that although mechanical irritation excited slight contractions in the muscles of a limb, whose nerves had been divided about a week before the death of the animal \*; yet none could be produced in them, by the influence discovered by Galvani. Instances might be adduced, in which the employment of this influence in physiological

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\* It is found, that the structure of a nerve is altered; even to the naked eye, when it has been divided for some time before the death of the animal.

fiological inquiries has already led to erroneous inferences, from our not being sufficiently acquainted with its laws.

The circumstances which seem chiefly to influence experiments, made on the irritability of frogs with the grofs test I employed, are, 1<sup>st</sup>, Their age, the irritability of young frogs being much more readily exhausted than that of such as are full grown. 2<sup>dly</sup>, Their death being sudden or lingering, the latter leaving the irritability more impaired than the former. 3<sup>dly</sup>, The time which the frogs are kept after being brought from the fields. The more vigorous frogs are, the more irritability their muscles possess. 4<sup>thly</sup>, Throwing ligatures around the limbs. If a tight ligature be thrown around a limb, and kept applied for twenty minutes, or half an hour, immediately



diately before the death of the animal, all the muscles beyond the ligature are found, after its death, quite void of irritability.

This cannot be attributed to the ligature pressing on the nerves of the limb, and cutting off its free communication with the brain, since dividing the nerves does not produce the same effect. It seems to depend on an accumulation of blood taking place in the muscles, (which are always found very red), owing to its return by the veins being prevented.

This fact suggests an experiment, by which it may be determined, perhaps, whether or not the irritability of the muscles be derived from the nervous system. For if it be found, that, when

the muscles of a limb are thus deprived of their irritability, (which they may readily be during the life of the animal), it can be restored, after all the nerves going to the limb are divided, there will then be little doubt of its being derived from some other source. I have made this experiment, but not in so satisfactory a manner, that any certain conclusion can be drawn from it.

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THE

THE doctrine of the sympathy of nerves has been so much employed in accounting for the effects of opium, that a few observations upon it here may not be improper. Although there is scarcely any doctrine in medicine at present more implicitly received, it seems far from being fully established\*.

The phenomena which have been referred

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\* The following opinions concerning this doctrine were laid before the Royal Medical Society of Edinburgh, and ordered to be inserted in their books, on the 1st of February 1794. I mention this circumstance, because a work has appeared since the above date, in which, although the author maintains very different opinions on this head, there are one or two hints thrown out, to which, it might be thought, I should own some obligation.

ferred to the sympathy of nerves, are those in which an involuntary motion, or a sensation, is produced in any part of the body by an irritation applied to the extremities \* of the nerves, not of that part, but of some other ; such as the motion of the diaphragm in sneezing, produced

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duced

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\* A sensation produced in any part, by stretching or compressing the trunk of the nerve which terminates in it, is no instance of the sympathy of nerves. If a nerve going to any part be compressed, the feeling of that part must be impaired. If a nerve be stretched, there must be a pain referred to its extremities, for the same reason that, were we to pull a muscle, we should excite a pain at its insertions. Is it a just inference from these facts, that an injury applied to the nerves of a stump will excite a pain referred to the extremity of the member that is lost ? Has not confounding these facts with others referred to the sympathy of nerves, to which they bear no analogy, tended to perplex this subject ?



duced by an irritation of the nares, a pain felt in the glans penis from an affection of the bladder \*," &c.

These phenomena, then, may be divided into two classes; those in which *sensation*, and those in which *motion*, is the result. I shall, in the first place, consider the former, because under it the more numerous set of facts are included; and because, what I shall say of this class will be found useful in speaking of the other.

The

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\* With regard to those cases of sympathy in which the muscles of involuntary motion only are concerned, they do not fall to be considered here; since, in the present state of our knowledge, there is not a shadow of reason for attributing them to any connection of nerves.

The following question is the first that presents itself, concerning which there can scarcely be two opinions. In what part of the system does that change take place, which is the immediate cause of sensation ?

The immediate cause of sensations, either exists in the various parts to which they are referred, demonstrating that the sensorium commune pervades the whole system ; or it does not, demonstrating that the sensorium commune is confined to a particular part of the system, to which every impression causing sensation is conveyed. Since one of these positions must be just, in order to establish either, it is sufficient to show, that the other is not. The question, then, resolves itself into this, Does the imme-

mediate cause of sensations exist in the parts to which they are referred ?

When a man complains of a pain in the toes, after the limb has been amputated, is the immediate cause of the sensation in the part to which it is referred, or elsewhere ? No body can hesitate in answering this question. We have, therefore, an unequivocal instance, in which the immediate cause of sensation does not exist in the part to which it is referred.

But this is not a solitary fact, it is a general law of the animal œconomy, that we continue to refer various sensations to any part of the body, which is suddenly lost for some time after it is so. The fact is as evident in the loss of a  
finger,

finger, or in that of a tooth, as in the loss of a limb. Nor can it be shewn, why the immediate cause of sensation should so exist in these cases, and not in all.

From direct experiment, then, the conclusion is unavoidable, that the immediate cause of sensations does not exist in the parts to which they are referred, but in some other ; that is, the sensorium does not pervade the whole system, but is confined to a particular part of it ; and having advanced thus far, we know, from numberless observations, that this part is lodged somewhere within the cranium in man, and, by analogy, in the animals that resemble man. In some animals it seems partly lodged in the spine. It is this part, then, which is meant by



the term *sensorium commune*, wherever it occurs in the present paper.

The next question which presents itself is, If the immediate cause of sensation exists in the *sensorium commune*, why do we very constantly refer the sensation to the part of the body on which the impression, causing it, is made \*.

When we look at the various objects that surround us, why do we refer one to the distance of two feet, another to that of three, and so on? For no other reason,

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\* The mode of reasoning employed in considering this question, though different, is similar to, and was suggested by, what Hartley says of the manner in which we refer sensations to particular parts of the body. See his *Theory of the Human Mind*.

reason, but that experience has taught us to connect certain sensations with certain distances. When we see two objects which we know to be nearly of the same tangible extension, for instance, two men, and yet observe, that the one occupies but the fourth of that part of the visible plain which is occupied by the other, we judge the former to be at twice the distance of the latter ; if the former occupy but the ninth part of that space occupied by the other, we judge him to be at three times the distance ; and so on. The degree of faintness, the number of intervening objects, and a few other circumstances, occasionally assist us when we judge of the distance of objects by the eye. But none of these circumstances are essentially connected with distance ; it is only experience which

has

has taught us to connect them in our minds.

Precisely the same thing takes place in the other case ; there is no particular sensation essentially connected with any particular part of the body ; but experience has taught us to connect certain sensations with certain parts \* : so that to the sensation arising from every impression, there is something as it were superadded, which we have constantly observed attend all impressions made on the same part ; and it is this which teaches us to refer the sensation to that part ; in the same manner as there is something, for instance,

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\* For the manner in which we at first discover the seat of impressions, see Hartley on the Human Mind, and others.



instance, the degree of faintness, super-added to the appearance of all bodies at the same distance, which teaches us that they are at that distance.

And as, in the latter case, according to a well-known law of the animal œconomy, we attend to the distance of an object, overlooking the means by which we acquire a knowledge of its distance; so, in the former case, we attend to the injured part, overlooking the means by which we determine its position with respect to other parts of the body.

Is it said, that we have a power of referring sensations to particular parts of the body, independent of experience? The following simple experiment is sufficient to convince us that we have not. I have frequently made the experiment,  
since



since I first heard of it from a gentleman of my acquaintance.

We refer sensations with little accuracy to parts of the body which we are not much accustomed to see, or otherwise distinguish from each other. If a person blind his eyes, and desire another to touch one of his small toes, he will find it quite impossible to tell which of them the person touches, and will not guess right much oftener than he would do, were the other touching one of four things quite unconnected with his body.

We arrive, then, at this conclusion, that the immediate cause of sensations exists in the sensorium commune; and that they are referred to the parts, on which the impressions causing them are made, by experience alone.

We

We have all perceived, that the sensation arising from a pretty strong impression is not confined to the very spot to which the injury is applied, but is felt, at the same time, in surrounding parts.

It is also a fact, that the more sensible any of the surrounding parts is, the more, in general, it partakes of the sensation. Thus, in a person labouring under the stone in the bladder, the whole hypogastric region is pained. But the end of the urethra, glans penis, and testicle, parts endowed with very keen feeling, partake more of the sensation than any other.

By how many injuries applied to distant parts, is the stomach affected, which is perhaps the most sensible part of the system?

Inflamed

Inflamed fores, where there is a morbid degree of sensibility, are excellent examples of the same thing. If any part near such a fore be injured, the pain is felt more acutely in the fore than in the other neighbouring parts \*.

But it is likewise a fact, that when any of the parts in the neighbourhood of that

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\* The pain in affections of the liver being referred to the shoulder, and not to the stomach, the more sensible neighbouring part, seems an exception to the general rule. But it appears from many instances, that those parts are most apt to sympathise, which lie nearly in the same line from the brain. This, it is more than probable, is owing to such parts being supplied with nerves from neighbouring parts of this organ. We meet with idiosyncrasy in this as in other functions of the system. I shall presently have occasion to mention an instance of this kind; many others might be adduced.



on which the impressiion is made, is a part of very acute feeling, while the injured part itself is one of comparatively dull feeling, the sensation excited in the former is often more intense than that excited in the latter.

We have instances of this in both the cases just stated : the pain excited in the fore is often more acute than that excited in the injured part, in its neighbourhood ; and that excited in the urethra, glans penis, and testicle, than the pain felt in the region of the bladder. When this takes place, as we attend to the stronger impressiion, and neglect the weaker, the former only is felt.

In all such cases, we refer the sensation from a less to a more sensible part ; yet it is not at all times wholly confined



to the latter ; for when we attend particularly to the seat of the impression, we generally feel a sensation there, as well as in the more sensible distant part ; but one so faint, that it is overlooked while the stronger sensation is present, except we endeavour to perceive it.

All that is here said is well illustrated by the following experiment, which I accidentally hit upon some years ago. I found, that by roughly irritating the umbilicus, a part endowed with very dull sensation, I could excite a pain at the end of the urethra \*. As the irritation

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was

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\* I mentioned this circumstance to a gentleman of my acquaintance, who, on pinching the umbilicus, felt a pain along a great part of the urethra. I have mentioned it to others, who experienced no such effect from irritating this part.

was increased, this pain gradually became very acute. There was also a dull sensation of general pain in the lower belly, similar to that produced when the testicle is slightly injured, which remained for some time after the irritation was withdrawn. Having made the experiment frequently in the space of ten or twelve minutes, I may observe by the bye, a considerable degree of sickness at stomach was produced, and a sensation I cannot well describe ; which was so disagreeable, that I have not since prevailed on myself to repeat this experiment.

I constantly observed, in making it, that when the pain at the end of the urethra was considerable, the irritation was not felt at the umbilicus, although I

I

could

could always perceive it, by bending my attention to this part.

Upon the whole, then, we find, that the sensation is not always confined to the part on which the impression is made ; that it is felt in surrounding parts, with various degrees of intensity, generally proportioned to their degrees of sensibility ; and that it is sometimes more acute in the more sensible neighbouring parts, than in that to which the injury is applied.

But it has been shewn, that the immediate cause of every sensation exists, not in the part to which it is referred, but in the sensorium commune ; and that the sensation is referred to the former, by experience alone.



Comparing these facts, the conclusion is unavoidable, that the phenomena, which are said to depend on the sympathy of nerves, as far as relates to those instances in which sensation only is concerned; proceed from certain changes induced on the sensorium commune, and depending on the two following circumstances; namely, different parts of the sensorium being endowed with different degrees of sensibility, and a change occasioned in one part being capable of inducing a similar change in some other; the sensations caused by such changes, being each referred to its corresponding part of the body, in the manner above explained.

The application of the principles just laid down, to explain particular cases, in which the phenomena in question take



place, is in general so evident, that it requires no illustration. I shall consider the only instance in which it is not so. One I have already had occasion to mention, in which we refer the sensation to a part that is separated from the body; and I shall take as an example of this, a person complaining of a pain in the toes, after the leg has been amputated.

Provided certain causes, capable of giving us a sensation, which we have been accustomed to refer to a certain part of the body, still continue to act, the sensation will be referred thither, whether the part itself exists or not, till a new experience overcome the former, and teach us not to refer any sensation to a part that is now lost.

It is evident from what has been said,  
that

that after the amputation of a limb, there still may exist in the body, causes capable of giving us sensations which we have been accustomed to refer to this limb; for we have been accustomed to refer to it, not only sensations from impressions made on the limb itself, but those from impressions made on parts in its neighbourhood. The pain excited by the irritation at the end of the stump, therefore, is referred to that part of the limb we have lost, as well as to the part which remains.

But it has been shewn, that of the parts in the neighbourhood of that on which the impression is made, those partake most of the sensation which are endowed with the keenest feeling. Of all the parts of the inferior extremities, the toes are the most sensible: on this account the

injury done to the limb is felt more severely in them than in any other part of it.

None of us would be surpris'd to find a person complaining of a pain in the toes, from a wound in any part of the leg, while it still remains attached to the body ; yet, if the facts which have been stated be just, (and that they are so cannot, I believe, be questioned), the pain, in both cases, is referred to the toes, for precisely the same reason \*.

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\* Speaking of a certain hypothesis, Dr. Darwin observes, in the 3d section of his *Zoonomia*, " There " is another objection, that at first view would seem " less easy to surmount. After the amputation of a " foot or a finger, it has frequently happened, that an " injury being offered to the stump of the amputated

limb ]

With regard to the cases referred to sympathy of nerves, in which motion is the result, it may be observed, we every hour see the sensorium affected by impressions made on the nerves ; and the consequence motion in various parts of

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“ limb, whether from cold, too great pressure, or  
 “ other accidents, the patient has complained of a  
 “ sensation of pain in the foot or finger that was cut  
 “ off. Does not this evince that all our ideas are ex-  
 “ cited in the brain, and not in the organs of sense ?  
 “ This objection is answered by observing, that our  
 “ ideas of the shape, place, and solidity of our limbs,  
 “ are acquired by our organs of touch and sight,  
 “ which are situated in our fingers and eyes, and  
 “ not by any sensations in the limb itself.”

But how are sensations from impressions made on the stump associated with any idea of the fingers or toes ? Such sensations have been associated with the



of the body, universally ascribed to the change produced in this part of the system. But why do we select certain motions, sneezing, vomiting, &c. excited by similar impressions, and alledge that they depend on other laws? Because the

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latter

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idea of that part at which the limb was amputated. Dr. Darwin observes, indeed, in the next paragraph, “ In this case the pain or sensation, which formerly  
 “ has arisen in the foot or toes, and been propaga-  
 “ ted along the nerves to the central part of the  
 “ sensorium, was at the same time accompanied with  
 “ a visible idea of the shape and place, and with  
 “ a tangible idea of the solidity of the affected limb:  
 “ now, when these nerves are afterwards affected by  
 “ any injury done to the remaining stump with a si-  
 “ milar degree or kind of pain, the ideas of the shape,  
 “ place, or solidity of the lost limb, return by asso-  
 “ ciation; as these ideas belong to the organs of  
 sight

latter motions are involuntary. They are not wholly so, however; both vomiting and sneezing can often for a certain time be interrupted by the will. Besides, they are frequently interrupted, and

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“fight and touch on which they were first excited.”

No farther supposition would seem requisite, were it ascertained, that after a leg is cut off, the irritation at the end of the stump is applied to the trunks of those nerves only that terminated in the part of which the patient complains, chiefly the toes. But we know that the irritation is applied to the cut ends of all the nerves which went to any part of the amputated limb; so that, were Dr. Darwin's explanation just, not the idea of the toes only, but that equally of every part of the limb, should be associated with the pain at the end of the stump.

and vomiting even produced, by a strong affection of the mind. And are there not other motions generally admitted to depend on an affection of the sensorium commune, which have the same right to be referred to the sympathy of nerves? Tickling the sides, or soles of the feet, excites violent and completely involuntary motions. Yawning too, and many other similar motions, might be adduced as instances of the same kind.

But laying this mode of reasoning aside, if it be granted, that the motions which have been referred to sympathy of nerves are not independent of the sensations which precede them, (and nobody, I believe, will assert that they are), it is a corollary from what was said of the cases of sympathy, in which sensation is the result, that these motions proceed

ceed from affections of the sensorium commune.

Dr. Monro, who has paid more attention to this subject than most other authors, was led, by many observations, to this conclusion, “ That, in general, the nerves of the body sympathise, not from their connection in their progress, but from their connection at their origin.” I would only go a step farther, and say, that the nerves always sympathise from their connection at their origin ; which is the same as saying, that no such thing as the sympathy of nerves exists, and that all the phenomena, which have been referred to this supposed law, depend on affections of the sensorium commune.

But



But granting (it may be said) that the immediate cause of all these phenomena exists in the sensorium commune, if it be found that those parts are most apt to sympathise, between which there is the most evident connection of nerves, the connection of nerves must be regarded as a mediate cause of the phenomena in question. But how slight, in many instances, is this connection between parts which sympathise most? And where do we find it so evident as between parts which very rarely sympathise? What part, then, do the nerves act in the production of these phenomena? No other than they act in the production of all phenomena in which they are concerned, that of conveying impressions to the sensorium, or of conveying a somewhat (to use Dr.

Monro's

Monro's expression, in the present state of our knowledge the best perhaps, we can use) from the sensorium to the muscles of voluntary motion.

APPENDIX.



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## A P P E N D I X.

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*EXPERIMENTS, made with a view to determine the manner in which Tobacco acts on the Living Animal Body.*

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THE following Experiments may be deemed an useful addition to this Paper, because they both tend to confirm the results of those which have been related, and to establish some points concerning the



the action of tobacco on the living animal body.

The solution which was used in these experiments was prepared by exposing two ounces of tobacco with six ounces of water, in a phial carefully corked, to a temperature of 90°. for twenty-four hours\*. It was then filtered, and near six ounces of a strong solution obtained, which appeared black in a common two-ounce phial.

A few drops of this solution were injected

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\* This mixture was exposed to the temperature mentioned for twenty-four hours only, as the active parts of tobacco are readily extracted by water, and I had found, from a former trial, that it is very apt to become putrid at so high a temperature.

jected into the heart in four frogs, through a hole made in the auricle. The heart instantly became paralytic, and the animals were seized with the most violent trembling, and a complete loss of sense and motion in the eyes and fore-limbs : in some, the head was drawn back ; and in all, every joint of the hinder-limbs was convulsively bent to the utmost ; just the contrary of what happens in the extremities, when a solution of opium is injected in the same manner.

The frog, I had found from another experiment, is affected precisely in this way when the cranium is perforated, and the solution immediately applied to the brain.

After securing the aorta in other four frogs, a few drops of the same solution

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were

were injected into the heart, through a hole made in the auricle. It was instantly deprived of motion; but, with an exception I am about to take notice of, the other symptoms, observed in the last experiment, did not supervene.

No trembling nor spasmodic contractions of the muscles took place; the frogs continued to move their fore-limbs and eyes, as long, and, in short, died in precisely the same way, as frogs do that die in consequence of the heart being cut out. In one of them, which was very large, the eyes moved when irritated for about two hours.

In the first frog used in this experiment, a circumstance occurred, which at first appeared quite unaccountable.

Its



Its eyes gradually lost their sensibility, till, in the space of about ten minutes, they could not by any irritation be excited to motion. This, however, they gradually recovered and preserved, as has been mentioned. While the eyes were thus affected, the fore-limbs also were to a considerable degree deprived of motion, which they too recovered.

These symptoms I could only attribute to a little of the solution remaining on my fingers, and the instrument employed in opening the thorax, which might have been conveyed to the mass of blood, and through this medium applied to the brain, before the aorta was secured. That this conjecture was just, appears from what happened to the other three frogs used in this experiment.



Having repeatedly washed my hands and the instrument with cold water, before I handled the next frog, very little of this affection was observed in it; and as it was allowed to lie about ten minutes after securing the aorta, the affection was at its height before the solution was injected into the heart, by which it was not in the least increased. It gradually went off, as in the former case.

Before touching the third frog used in this experiment, I washed my hands and the instrument with warm water and soap, which entirely prevented any affection, either of the eyes or fore-limbs, in it. Neither did this occur in the last frog on which the experiment was made, when I had not been previously handling the solution.

I take notice of these circumstances, because they not only shew, how small a quantity of tobacco is capable of affecting this animal, and how readily it is received into the mass of blood, but also suggest a necessary precaution in making such experiments.

The state of the muscles after death was not examined in the first frog used in these experiments ; in the other seven, they contracted readily, on wounding the nerves which terminate in them, except in one, which was very young, and which had lain dead a considerable time before the state of its muscles was examined.

Left it should be said, that interrupting the circulation in the latter experiment prevented the tobacco producing

the effects observed in the former, the following was made.

After securing the aorta by ligature, and permitting the blood to escape, by wounding the auricle in three frogs, and cutting out the heart of a fourth, the cranium of each was perforated, and as much of the solution as possible applied to the brain.

They were all immediately seized with the most violent trembling; their forelimbs became paralytic, and their eyes fixed precisely as happened when the solution of tobacco was thrown into the heart, without previously securing the aorta. Their limbs contracted readily after death; on stimulating the nerves that go to them.



When a tube, containing a solution of tobacco, is forced along the spinal marrow, the hinder-limbs are instantly rendered paralytic, as the fore ones are when the solution is applied to that part of the brain which is lodged within the cranium; for some of Dr. Monro's observations, as well as this experiment\*, prove, that at least part of that portion of the brain which supplies the hinder-limbs in the frog, is lodged in the spine.

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\* This experiment, compared with the following, also proves another circumstance, that a much larger proportion of tobacco, when it is received into the system by means of the absorbents, is sent to the brain, than to the spinal marrow. This indeed we might, *a priori*, have expected from the great quantity of blood sent to the former.



The following experiment was made, to shew the comparative effects of tobacco, applied to the intestines of the entire frog, and to those of the same animal with the heart cut out ; where it can only act through the medium of the nerves of the part to which it is directly applied.

The first pair of frogs on which the experiment was made, were young, and very nearly of the same size : they were equally vigorous. Into the intestines of the larger, without removing the heart, twenty-eight drops of the solution were injected, the greater part of which was returned.

This frog was not examined till forty-two minutes after the injection of the solution ; it was then found without any  
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sign of life, except that, on suddenly letting fall the hinder-limbs, they were seized with a trembling motion, which lasted a few seconds. No motion could be excited in the eyes, and the fore-limbs were quite paralytic.

The heart of the other frog was removed, and twenty-two drops of the same solution injected into the intestines, very little of which was returned. This frog was affected with no trembling. It moved its eyes, when they were irritated, seventy-three minutes after the injection of the solution, and retained the motion of the fore-limbs, as long as that of the hinder ones.

On irritating the nerves after death, the muscles contracted readily in both  
these

these frogs. More of the solution was found in the latter than in the former.

The second pair were also young : they were of the same size, and equally vigorous.

Into the intestines of the first, without removing the heart, twenty-three drops of the same solution were injected ; the half at least was returned. Twenty-two minutes after the injection of the solution, this frog was found in exactly the same situation in which the first of the last pair was found at the expiration of forty-two minutes. After removing the heart of the other, twenty-three drops were thrown into its intestines ; fifty-eight minutes after the solution was injected, it moved its eyes when they were irritated. It died in the same manner as the second  
of



of the former pair. The irritability of the muscles in both remained after death.

Third pair. The result of this experiment in all respects resembled that of the last.

The fourth pair were full grown, and equal in size and vigour. The result of this experiment was again similar to that of the foregoing. The entire frog soon became affected with violent trembling. Fourteen minutes after the injection of the solution, no motion could be excited in the eyes, and the fore-limbs were paralytic. The other died as the second of the other pairs did. It moved its eyes eighty-nine minutes after the solution was injected.



As a large quantity (50 drops) was thrown into each of these frogs, the intestine gave way ; so that the solution got into the cavity of the abdomen ; and in the latter, part of it escaped by the opening at which the heart was extracted. Contractions were readily excited in the muscles of both after death.

The fifth pair were likewise full grown, and both uncommonly large. The one whose heart was cut out was rather smaller than the other. They were equally vigorous. Sixty-four drops of the solution were injected into the intestines of each of them ; which in this case also were ruptured in both frogs. None of the solution, however, was returned by the opening made for extracting the heart. In six minutes the fore-limbs of the entire frog were paralytic, and no motion could

could be excited by irritating its eyes; the hinder-limbs were affected with very violent trembling, and at times with strong spasms, resembling those induced by opium. I have observed this in a less degree in other instances, when tobacco was thrown into the intestines of the entire frog. The muscles of the hinder-limbs of this frog were found, after death, almost quite void of irritability.

As for the other, it retained all its motions for fifty-three minutes after the solution was injected; those of the fore-limbs as perfectly as those of the hinder ones: its eyes moved, when irritated, nineteen minutes longer; and its muscles contracted after death with unusual force.

All the frogs used in this experiment became languid soon after the injection of the solution. In eight or ten minutes, however, they were considerably less so ; precisely as happened in a similar experiment made with opium.

Whether the heart be previously removed or not, slight convulsive twitchings (chiefly on the back) are sometimes observed immediately after injecting a strong solution of tobacco into the stomach and intestines, or cavity of the abdomen, of a frog, resembling those which often take place in the human body, when a violent topical irritation is present. They are only to be perceived for a minute or two after the injection of the solution.

From the foregoing experiments with  
tobacco



tobacco, then, it appears, that the symptoms which it produces, when thrown into the heart, are the same with those excited by its immediate application to the brain: that these symptoms, when the tobacco is exhibited in the former way, proceed from no action of the tobacco on the nerves of the heart, but from its being conveyed through the aorta, and immediately applied to the brain; since they do not follow its injection into the heart, when the aorta is previously secured by ligature, although it was found, that interrupting the circulation does not unfit the nervous system from undergoing the change necessary for the production of such symptoms. It also appears from these experiments, that tobacco produces the same effects, though more slowly, when thrown into the stomach and intestines, as when  
 thrown



thrown into the heart ; that in the former case, as in the latter, they are still to be ascribed to the tobacco being received into the sanguiferous system, and immediately applied to the brain ; and that the effects of this drug, when it acts merely on the nerves of the part to which it is applied, do not essentially differ from those of any strong topical irritation. It may also be collected from these experiments, that the presence of tobacco in the system, like that of opium, only affects the irritability of the muscles of voluntary motion, when it produces convulsions in them ; *i. e.* when it is applied in considerable quantity to the brain. It appears, therefore, that the *modus operandi* of tobacco on the living animal body is in every instance analogous to that of opium.

May not poisons, in general, be divided into two classes : The first comprehending those which, applied to the sentient extremities of the nerves, produce effects on the system in general, not essentially different from the effects of mechanical irritation ; but which seem incapable of any other action through the medium of the nerves, although applied to them after laceration ; their effects on the system, when infused into a wound, differing only in degree from those produced by injecting them into any of the cavities of the body ; such are opium, tobacco, and a great variety of other poisonous drugs : The second class comprehending the poisons which seem less apt to affect the sentient extremities of the nerves in the sound state, but, applied to lacerated nerves, produce

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through them effects essentially different from those of mere topical irritation; such are the poison of the viper, that of rabbit animals, and some others?